REMARKS

Applicant respectfully requests reconsideration of the present application in view of the reasons which follow.

Claims 3-5 and 14 are pending in this application.

Rejection under 35 USC § 112, second paragraph

The examiner has rejected claims 3-5 and 14 for failing to point out and distinctly claim the subject matter of the invention.

First, applicant argues that the claims specify that the "artificial amino acid residues" do not occur in nature. Additionally, in the specification on page 12, lines 29-31, "artificial amino acid sequence.....refer[s] to those amino acid sequences that cannot be found in nature."

Separately, applicant argues that the specification on page 13, lines 10-19 describes a "primary antibody" as a humanized antibody subjected to amino acid substitution and having a biological activity equal to or higher than that of the mouse antibody. The specification continues to refer to this antibody as the end product of conventional humanized antibody techniques.

Continuing, on page 13, line 20 – page 14, line 11 describes "the homology search for the FR of a primary design antibody" as a search through FR databases for a natural FR that maintains the amino acid residue of the primary design antibody.

Applicant submits that claim 14 is definite as it recites that a "...homology search using a database of amino acid sequences of FRs naturally occurring in human antibodies..." which is compared to the FR amino acid sequence of the primary design antibody. Step (d) recites that FRs with high homology are selected.

In view of the foregoing arguments, applicant respectfully submits that all of the indefiniteness rejections have been addressed and the specification defines the claim language, and therefore a withdrawal of these rejections is respectfully requested.

Rejection under 35 USC § 103(a)

The examiner rejected claims 3-5 and 14 as being unpatentable over Sato et al. in view of Queen et al.; Co et al. in view of Queen et al.; and Roguska et al. in view of Queen et al. Applicant argues that these prior art methods do not result in a completely humanized antibody. According to the prior art, a CDR-grafted antibody is prepared by selecting a mouse monoclonal antibody (MAb), selecting a mouse framework region (FR), replacing a selected human constant domain region (CDR) with a mouse MAb CDR region, and modifying the human FR region with amino acids from the mouse FR region to improve binding. The resulting antibody is then analyzed for its crystalline structure, and amino acids in the FR, which are expected to be present on the surface of a modified humanized antibody are selected. Those identified surface amino acids that are considered to be immunogenic are replaced with corresponding amino acids in human FR. Importantly, the amino acid residues not present on the surface of the modified humanized antibody are not replaced.

Applicant submits that the present invention, unlike the prior art, results in fully humanized antibodies. Applicant further asserts that the additional steps in its method of making humanized antibodies distinguish their invention from the prior art. Similar to the prior art, step 1 of the present invention's process creates a modified humanized antibody by substituting one or more amino acid residues essential for antigen-binding activity. However, unlike the prior art the modification of the antibody does not stop here. After the immunogenic surface amino acids have been replaced with the corresponding amino acids in the human FR, steps 2 and 3 of the present application select human FRs having high homology with the FR of the primary antibody selected. In step 4, from these homologous FRs, an FR which contains the essential amino acids at the essential positions identified in step 1 is selected. Therefore, the end result is an antibody comprising a FR that is completely the same as the FR of a human antibody, while maintaining the binding ability to the antigen. Applicant submits that the prior art fails to suggest this method of obtaining a completely humanized monoclonal antibody.

In light of the foregoing arguments, applicant argues that the present invention is not obvious from the teachings of the cited reference.

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

If any fees are due in connection with the filing of this Amendment, please charge the fees to our Deposit account No 19-0741. If a fee is required for an extension of time under CFR § 1.136 that is not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date July 15, 2003

By _____
Reg. No. P-54,425
FOR: Harold C. Wegner
Attorney for Applicant
Registration No. 25,258

FOLEY & LARDNER
Customer Number: 22428
22428
PATENT TRADEMARK OFFICE
3000 K Street, N.W., Suite 500
Washington D.C. 20007-5109
Telephone: (202) 672-5569
Facsimile: (202) 672-5399